

Study Group – R/R ALL

There is still insufficient data about the proper bridging therapy management before CAR T cell therapy. This study group strives to understand the impact of low- and high-intensity bridging regimens on a variety of outcome parameters.

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Presentation: Dr. Maike Breidenbach, LMU Munich

Concept & Achievements

The R/R ALL group attempts to develop a guideline for the proper management of bridging therapy prior to antiCD19 CAR T cell therapy through a multinational, retrospective data collection and consensus workshops.

We defined the following milestones:

- » **development of a guidance for multimodal bridging therapy**
- » **set-up of registry for children and young adults with R/R ALL in Bavaria and beyond**
- » **analysis of markers for later response to immunotherapy approaches**
- » **preparing and defining a future GCP clinical trial and set-up of structures for the conduction of the trial**

Milestone 1: Guidance for multimodal bridging therapy

In October 2022, we set up a **consensus workshop** on bridging therapy prior to CAR T cell therapy for R/R ALL patients. Experts from Germany, Austria and Switzerland were invited to discuss. This led to a **publication**, which is currently **under revision**.

Milestones 2 and 3: Set-up of registry for children and young adults with R/R ALL and analysis of markers for later response to immunotherapy

See graphical abstract (Figure 1). Performed treatments were classified into the categories **1) no systemic therapy**, **2) low-intensity** and **3) high-intensity therapy** (Figure 2). Data analysis is almost done and results are shortly before publication.

Milestone 4: Preparing and defining a future GCP clinical trial and set-up of structures for the conduction

Due to the fact that we included further sites beyond Bavaria, we first focused on the execution and analysis of the large-scale registry. Hence, we have not started with this milestone, yet. Planning a GCP trial will have to rely on the registry results.

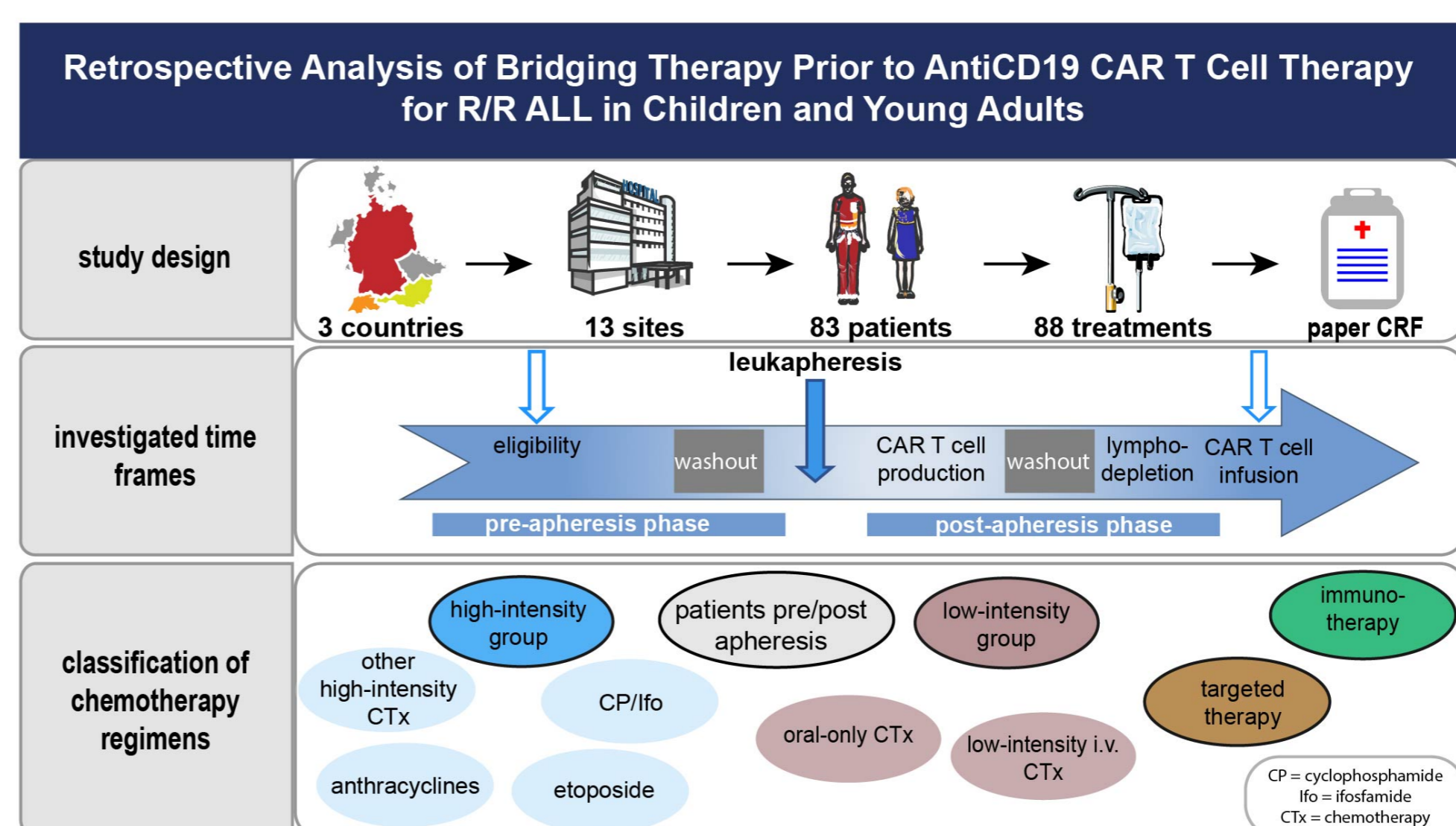


Figure 1: graphical abstract *

Major results of the registry:

- patients receiving a high-intensity bridging therapy had a significantly higher tumor burden at time point of eligibility defined by blasts in bone marrow and by measurement of minimal residual disease (MRD)
- tumor burden within the three groups converged over the time of bridging therapy (Figure 3)
- at time of lymphodepletion, patients in the high-intensity group showed a significantly lower performance status than patients in the low-intensity/no systemic therapy group
- ... and suffered significantly more often from bacterial adverse events and mucositis
- overall and disease-free survival did not differ significantly between groups.

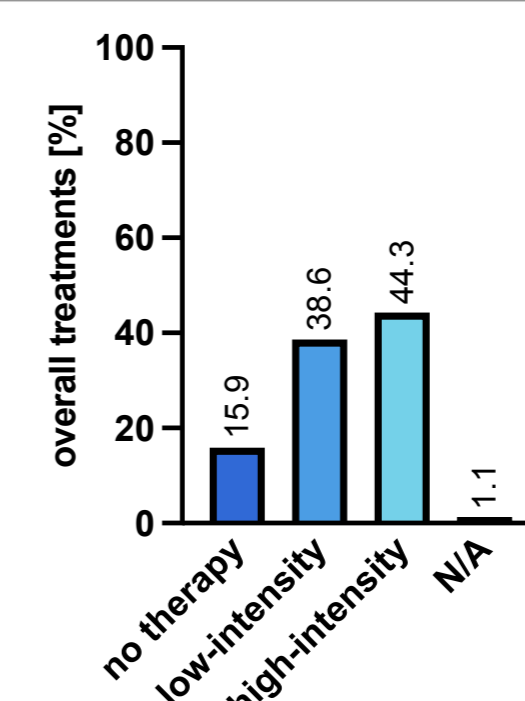


Figure 2: distribution of bridging therapies

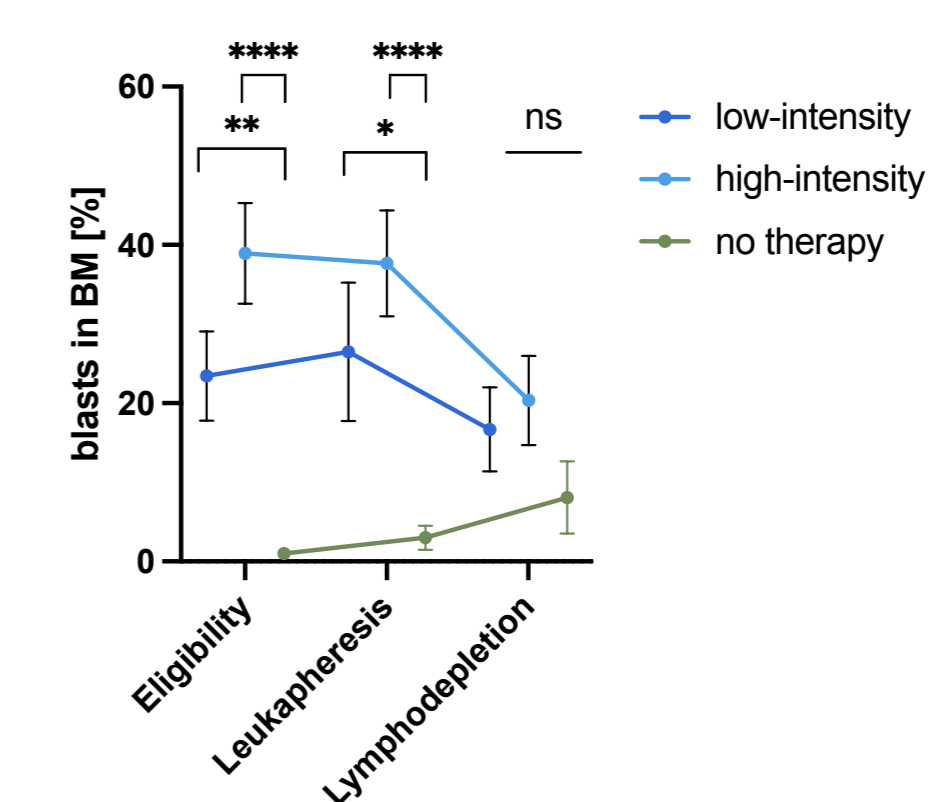


Figure 3: blasts in bone marrow preliminary data

Future Milestones

- » **Data publication until end of 2023**
- » **Preparation of a GCP-study**

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